

# Clinical Update on Neurosyphilis and Ocular Syphilis

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# Disclosures

- Nothing to disclose

# Learning Objectives

At the end of this presentation, attendees will:

1. Assess all patients who have syphilis, regardless of stage, for neurologic and ocular symptoms and signs
2. Recognize signs and symptoms of neurologic and ocular syphilis
3. Refer all syphilis patients with neurologic and/or ocular signs or symptoms for immediate further evaluation

# CDC April 2015 Clinical Advisory: Ocular Syphilis Alert- CA, WA, other states

- 24 cases majority HIV-infected MSM
  - Few HIV-uninfected men and women
  - Significant sequelae including blindness
- **Be aware of ocular syphilis:**
  - **Symptoms may include:** loss of vision, floaters, a blue tinge in vision, flashing lights and blurring of vision
- **Careful neurologic exam in syphilis patients**
- **Patients with syphilis and ocular complaints need immediate ophthalmologic evaluation!!!**
- **LP should be performed in patients with syphilis and ocular complaints**
- Prior research has documented neuropathogenic strains
  - ?unknown if oculo-tropic strain role in these cases

**Let's begin with a case**

# MSM with Rash & Blurry Vision

- 31 y/o MSM, methamphetamine use
- Symmetric macular rash on trunk and palms
- 1 month of blurry vision
- Feels generally unwell
- No meds, allergies or travel



# Diagnostic Work-up

- Ophthalmologist diagnosis: Retinitis
- Rapid HIV positive (CD4 50, VL 75,000)
- Normal CBC, electrolytes
- Neg PPD
- Neg RPR



## What might explain this patient's rash and ocular manifestations??

- 1) Acute HIV rash with CMV retinitis
- 2) Prozone phenomenon and ocular syphilis
- 3) Rash and retinitis have separate etiologies
- 4) None of the above



# Secondary Syphilis w/ocular involvement + Prozone

- Repeat RPR 1:1024
- Patient initial RPR- False Negative
- Retinitis is manifestation of Ocular Syphilis



# Ocular Syphilis



# Secondary Syphilis with Ocular Manifestations

- Lumbar Puncture Findings
  - CSF VDRL 1:16
  - RBC 6, WBC 80 (93% L)
  - Glucose 39, Protein 100
- Evidence of Neurosyphilis

# What stage(s) of syphilis involves the eye?

- All stages of syphilis can involve the eye.
- Eye involvement tends to occur most frequently in secondary syphilis and late syphilis

# What part of the eye is involved?

- **Every** part of the eye can be involved during **any** stage of the infection
- The vast majority of eye problems associated with syphilis are also associated with many other infectious and non-infectious diseases.
  - In other words, there are almost no eye findings that are absolutely specific for syphilis

# Ocular Syphilis

## Manifestations:

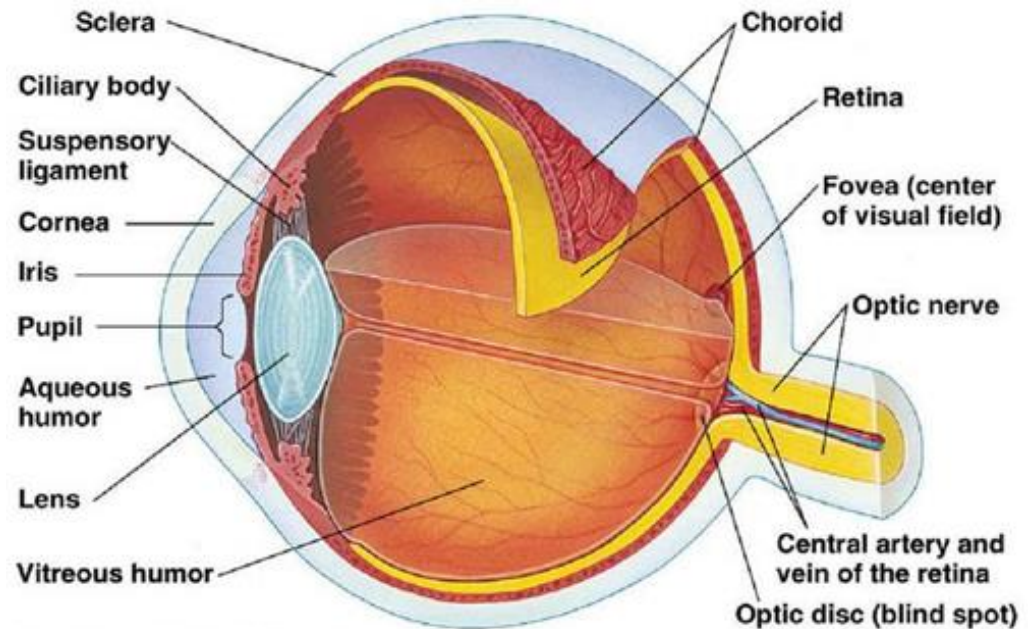
- Conjunctivitis, scleritis, and episcleritis
- **Uveitis**: anterior and/or posterior
- Elevated intraocular pressure
- **Chorioretinitis**, retinitis
- Vasculitis

## Symptoms:

- Redness
- Eye pain
- Floaters
- Flashing lights
- Visual acuity loss
- Blindness

## Diagnosis:

- Ophthalmologic exam
- Serologies: RPR, VDRL, treponemal tests
- Lumbar puncture



*Slide courtesy of Sarah Lewis, MD*



# *J.Clin Neuro-ophthalmol. 3:197-203, 1803*

## Ocular Manifestations of Syphilis

### Lids

- Chancre
- Gumma
- Tarsitis
- Ulcerative blepharitis

### Cornea

- Interstitial keratitis
- Ulcers
- Deep, punctate keratitis
- Keratitis profunda
- Keratitis punctate profunda
- Keratitis linearis migrans
- Gumma

### Retina and Vitreous

- Chorioretinitis-pseudoretinitis, pigmentosa, salt and pepper fundus
- Perivasculitis
- Central retinal artery/vein occlusion
- Cystoid macular edema
- Vitritis

### Conjunctiva

- Chancre
- Papular syphilides
- Gumma

### Sclera

- Episcleritis
- Scleritis
- Gumma

### Optic Nerve

- Neuritis
- Perineuritis
- Neuroretinitis
- Gumma

### Orbit

- Periostitis
- Gumma

### Iris and Ciliary Body

- Roseolae
- Papules
- Gumma

### Motility Dysfunction

- Oculomotor, abducens, trochlear paresis – associated with basilar meningitis
- Periodic alternating nystagmus

### Anterior Chamber Hypopyon

### Lens

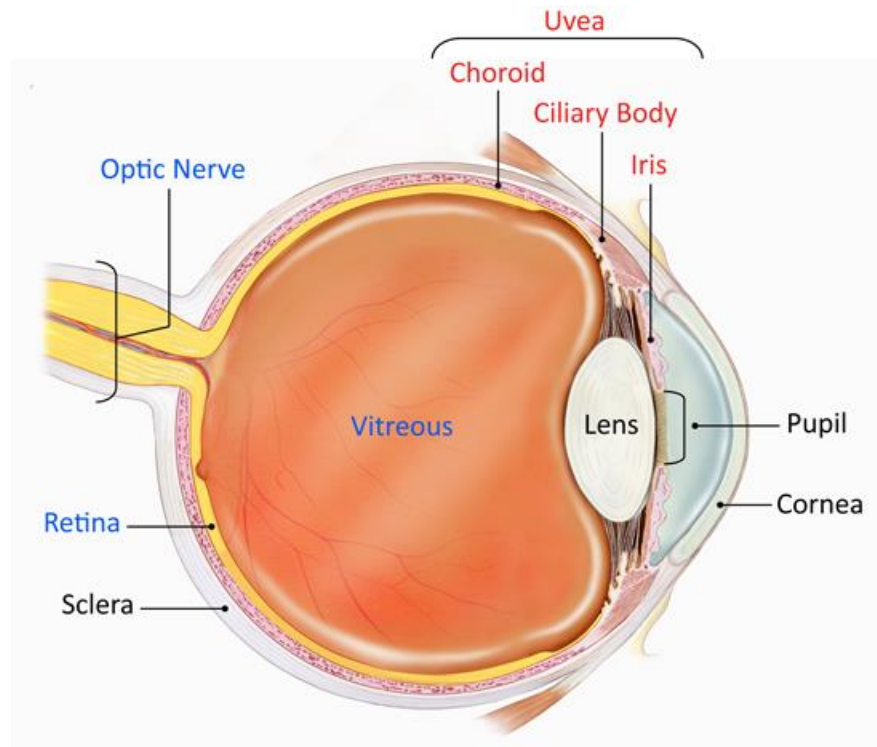
- Capsular rupture and necrotizing cortical inflammation (congenital syphilis)
- Dislocation

### Pupils

Light-near dissociation

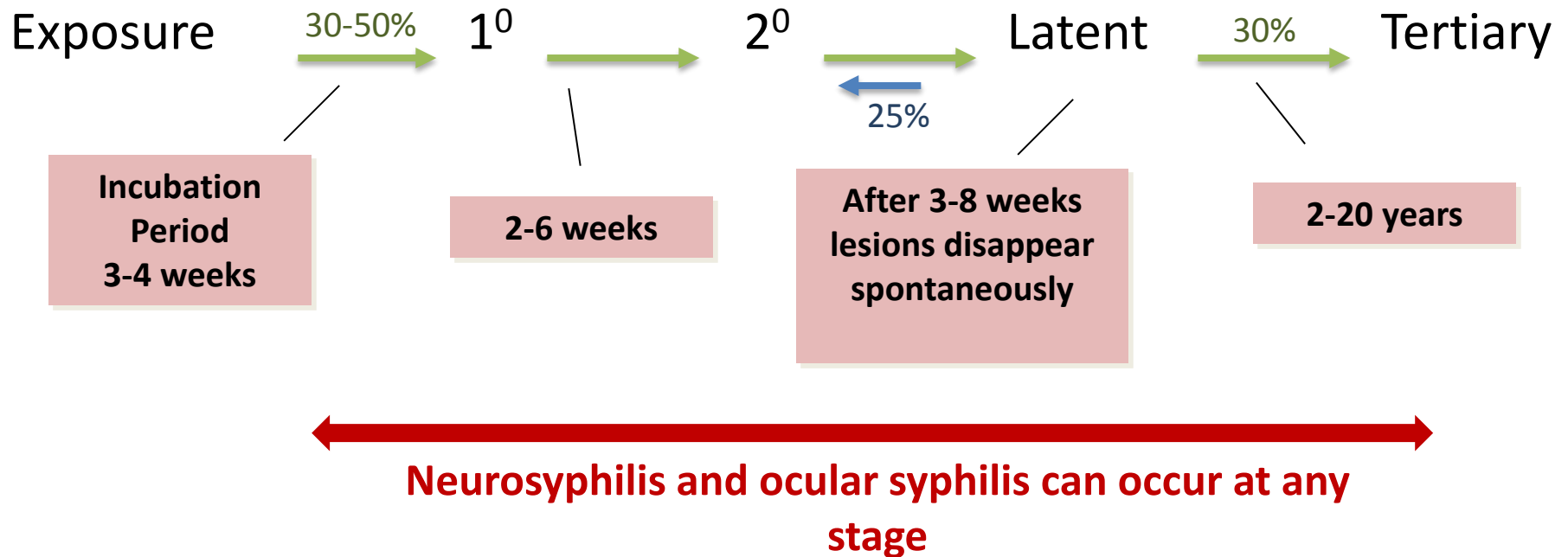
# Are ocular syphilis and neurosyphilis the same thing?

- No, they are separate entities but there is a lot of overlap





# Syphilis Natural History



# Symptoms: Questions to Ask

## SYMPTOMS OF NEUROSYPHILIS

- |   |                              |                             |
|---|------------------------------|-----------------------------|
| 5) Have you recently been having headaches?   | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| 6) Have you had new-onset weakness in any part of your body (including your arms, legs, or face)? | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| 7) Have you had problems walking?   | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| 8) Have you had problems with memory or confusion?  | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| 9) Do you feel (or have you been told) that your personality has changed?                         | <input type="checkbox"/> Yes | <input type="checkbox"/> No |

*Providers should consider evaluation and treatment for neurosyphilis in patients with new-onset of headaches (or headaches that are different from their usual headaches); new and persistent change in personality, memory or judgment; new numbness or weakness in the face, arms or legs; and/or new gait incoordination.*

# Symptoms: Questions to Ask

## SYMPTOMS OF OCULAR SYPHILIS

- |  |                              |                             |
|--|------------------------------|-----------------------------|
| 1) Have you recently had a change or blurring in your vision?      | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| 2) Do you see flashing lights?                                     | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| 3) Do you see spots that move or float by in your field of vision? | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| 4) Have you recently had pain or redness in the eyes?              | <input type="checkbox"/> Yes | <input type="checkbox"/> No |

*Providers should consider evaluation and treatment for ocular syphilis in patients with new changes in vision, including loss of vision, blurring, seeing spots or flashing lights and pain and/or redness in one or both eyes.*

# Who do we diagnose with ocular syphilis?

- Ocular signs and symptoms in a person who has syphilis
  - Most diagnoses are presumptive
  - Most patients will have positive serological tests
    - In patients with late ocular syphilis, 30% may have a NEGATIVE serum RPR but all will have a positive serum treponemal test
    - VERY rarely, someone with early syphilis (primary stage) will have negative syphilis serologies (both treponemal and RPR) and eye symptoms

# Do you need to do an LP in someone who only has eye symptoms and no neurological symptoms?

- YES, and here's why:
  - If the CSF VDRL is positive in someone who has eye symptoms, you can make a DEFINITIVE diagnosis of ocular syphilis (that's really the only way to make a DEFINITIVE diagnosis)
  - Up to 70% of patients with ocular syphilis will have evidence of neurosyphilis on LP
  - If they have evidence of neurosyphilis, the clinicians will need to follow them with LPs every 6 months to make sure they are responding to therapy

# What should you do if you suspect someone has ocular involvement?

- In rare cases, syphilis of the eye can progress very rapidly and cause blindness
- If one suspects that eye symptoms are due to syphilis, patients must be evaluated by an ophthalmologist quickly
  - If you don't have access to an ophthalmologist, then patients need to be referred to a local ER
- If the ophthalmologist finds evidence of eye involvement, the patient will likely need a LP

# How do we treat ocular syphilis

- Use the same regimen as neurosyphilis EVEN IF THE LUMBAR PUNCTURE IS NORMAL (remember, 30% of patients with ocular syphilis will have a normal lumbar puncture)
- One should be careful NOT to delay antibiotics while waiting for a lumbar puncture to be done

# Ocular Syphilis / Neurosyphilis Treatment

- Recommended regimen:
  - Aqueous Crystalline Penicillin G 18-24 mu IV daily administered as 3-4 million units IV q 4 hr for 10 -14 days
- Alternative regimen:
  - Procaine Penicillin G 2.4 mu IM daily plus Probenecid 500 mg PO q d, both for 10-14 days

CDC 2015 STD Treatment Guidelines



# **Will patients with ocular syphilis get better with antibiotic treatment?**

- Yes, the majority of patients will get better with antibiotic treatment if antibiotics are not significantly delayed
- Some patients, particularly those with late ocular syphilis, may not improve. The goal of therapy in these patients is to stop further progression of disease

# *T. Pallidum* strains associated with neurosyphilis?

- *T. Pallidum* DNA from 83 patients evaluated for neurosyphilis (Seattle)
  - 21(50%) of 42 patients with one strain type (14d/f) had neurosyphilis (  $P = .02$  )
  - 10 (24%) of 41 patients with the other 7 strains had neurosyphilis
- Rabbit studies
  - Animals infected with 14a/a strain and 14d/f strain had greatest degree of neuroinvasion.
- Further study needed

*Marra et al. JID 2010*

*Tantalo et al. JID 2005.*

# Ocular Syphilis: Ongoing Questions and Challenges

- Lack of clarity whether this represents:
  - outbreak of a more neuro/ocular-tropic syphilis strain  
*versus*
  - increased awareness of a known complication of syphilis in the setting of rising number of syphilis cases
- Limitations of current surveillance system to detect/record ocular syphilis cases

## In summary

- **Clinicians should be aware of ocular syphilis and screen for visual complaints in any patient at risk for syphilis.**
  - Risk factors for syphilis include having sex with anonymous or multiple partners, sex in conjunction with illicit drug use, or having a partner who engages in any of these behaviors.
- **Assure that all patients diagnosed with syphilis, or suspected of having syphilis, are evaluated for ocular and neurological symptoms.**
- **Refer patients with positive syphilis serology and either ocular or neurological signs or symptoms immediately for: ophthalmologic evaluation; evaluation for lumbar puncture with CSF examination; and possible hospital admission and IV therapy.**

# In summary

- **Obtaining a lumbar puncture is ideal, but treatment should NOT be delayed while waiting for a lumbar puncture.**
- **Manage ocular syphilis according to current CDC treatment guidelines for neurosyphilis** (Aqueous crystalline penicillin G IV or Procaine penicillin IM with Probenecid for 10-14 days; see <http://www.cdc.gov/std/tg2015/syphilis.htm>).
- **Test all patients with syphilis for HIV if status is unknown or previously HIV-negative.**
- **Report all cases of ocular syphilis to your local health department within 24 hours of diagnosis.**
  - The case definition for an ocular syphilis case is as follows: a person with clinical symptoms or signs consistent with ocular disease (i.e. uveitis, panuveitis, diminished visual acuity, blindness, optic neuropathy, interstitial keratitis, anterior uveitis, and retinal vasculitis) with syphilis of any stage.

March 13, 2015 | by Staff reports

## Gay men blinded by ocular syphilis outbreak

148

94

3

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Seven cases of ocular syphilis have been reported in San Francisco, five among MSM and six of whom were HIV-positive, the AIDS Healthcare Foundation reports.

## Cases of ocular syphilis on the rise

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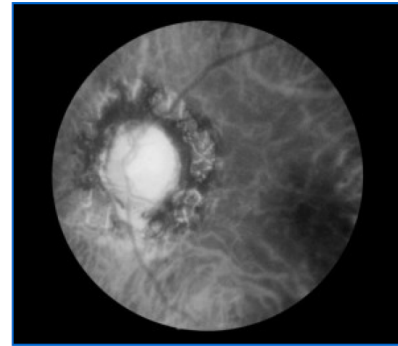
philly.com

Did you know that syphilis can affect your eyes? iStockphoto

## Syphilis: Washington reports 6 ocular syphilis cases in past month, blindness reported in two

Posted by [Robert Herriman](#) on January 24, 2015 // [7 Comments](#)

Since mid-December 2014, the Washington Department of Health has reported six cases of ocular syphilis, or syphilis of the eyes, causing blindness in at least two patients.



This funduscopy image reveals the effects of late neuro-ocular syphilis on the optic disk and retina/CDC

[Outbreak News Today](#)

## LA County Health Officials ID 2 Possible Cases Of Ocular Syphilis

March 10, 2015 12:02 PM

[View Comments](#)



CBS

(Photo credit: Thinkstock)

**Thank you**